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Review

Comparison of short-term clinical outcomes of intra-articular injection of micro-fragmented adipose tissue and stromal vascular fraction cells for knee osteoarthritis treatment: A retrospective single-center cohort study

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A B S T R A C T

Background: Stromal vascular fraction (SVF) cells and micro-fragmented adipose tissue (MFAT) have potential for treating knee osteoarthritis (OA), but their efficacy has not been compared. This study aimed to compare the clinical outcomes of SVF and MFAT for knee OA. We hypothesized that SVF provides stronger short-term effects, while MFAT offers more sustained benefits.
Methods: A retrospective single-center cohort study was conducted on patients with knee OA, with 36 SVF and 36 MFAT cases selected through propensity score matching between September 2017 and February 2022. Patients with KL grades I–IV varus knee OA, significant pain (VAS $\geq$40), and functional impairment despite conservative treatments were included. Those with knee trauma, severe bony defects, infections, genu valgus, osteonecrosis, rheumatoid arthritis, or severe deformities were excluded. Clinical outcomes were assessed using the visual analog scale, KOOS, knee range of motion, extension/flexion strength, and MRI T2 mapping.
Results: SVF and MFAT groups demonstrated significant improvements in VAS ($p < 0.01$ for both groups). Both groups showed notable improvements in extension angle, extension/flexion muscle strength, and KOOS, with no significant differences between them. However, the MFAT group demonstrated significantly greater improvement in flexion angle compared to the SVF group ($p = 0.03$). No serious adverse events were reported. T2 mapping showed significant improvements in cartilage quality in both groups, with the MFAT group demonstrating superior improvements in specific lateral regions. Responder rate in SVF group initially improved but declined over time; however, the MFAT group showed sustained improvement from six months onward.
Conclusion: T2 mapping revealed that MFAT had better cartilage preservation than that of SVF cells in less-loaded areas, with a potentially longer-lasting therapeutic effect. These findings offer important insights for clinicians to tailor treatment strategies based on patient needs and disease progression.

Contents

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1. Introduction

Knee osteoarthritis (OA) is a degenerative joint disease characterized by pain, inflammation, and functional impairment, significantly impacting patients' quality of life [1]. Adipose-derived mesenchymal stem cells (AD-MSCs) have garnered attention for their regenerative potential in treating knee OA due to their multipotency and ability to modulate inflammation [2,3]. These cells secrete anti-inflammatory cytokines, including interleukin (IL)-10, transforming growth factor beta (TGF-β), and IL-1 receptor antagonist, contributing to cartilage preservation and symptom relief in knee OA [4,5]. Moreover, AD-MSCs enhance angiogenesis and regulate immune responses, providing a comprehensive therapeutic approach [6].

Despite the known therapeutic potential of AD-MSCs, clinical outcomes vary significantly depending on the specific formulation used. Among these, stromal vascular fraction (SVF) cells and microfragmented adipose tissue (MFAT) represent two distinct preparations with unique properties [7,8]. SVF cells are rich in diverse cellular components and exhibit potent anti-inflammatory effects [9], while MFAT retains its structural matrix, potentially enabling sustained growth factor release [10]. These differences suggest that SVF may provide strong short-term effects, whereas MFAT might sustain therapeutic benefits over a longer period [9,10].

Although individual studies have demonstrated the benefits of each formulation [11,12], no research has directly addressed their comparative performance, particularly regarding the duration and sustainability of their effects. Clarifying this uncertainty is essential to optimize patient management and guide clinical decision-making. Therefore, this study aimed to compare the clinical outcomes of SVF and MFAT for knee OA, focusing on their therapeutic effects over time. We hypothesized that SVF provides stronger short-term relief, whereas MFAT offers more sustained benefits, potentially resulting in superior long-term outcomes.

2. Materials and methods

2.1. Study design

This retrospective single-center cohort study was designed to evaluate and compare the clinical outcomes of SVF cells and MFAT in patients with knee OA. An orthopedic surgeon (S.S) with more than 20 years' experience in orthopedics, including over eight years specializing in regenerative therapy for knee osteoarthritis, provided a comprehensive explanation, obtained informed consent, and performed all procedures, including the harvesting, preparation, and injection of the treatment. Ethical approval for the study was obtained from the Review Board for Human Research of Sobajima Clinic (reference numbers: SC002-1 M and SC002-2 M) and the Kobe University Graduate School of Medicine (reference number: 170181). All participants provided informed consent to participate in the study. The study adhered to the STROBE guidelines for reporting observational studies. Treatments were administered between September 2017 and February 2022, and the data were collected in the orthopedic surgery department of a clinic which has a regenerative medicine department. The inclusion criteria focused on patients with knee OA, primarily grades II–IV, as per the Kellgren-Lawrence (KL) classification, who exhibited varus knee alignment and significant pain (VAS $\geq$40) despite conservative treatments. Grade I cases were only included if functional impairment was significant and unresponsive to conservative management. The exclusion criteria included history of knee-joint trauma, presence of severe bony defects, active or previous joint infections, genu valgus, osteonecrosis, rheumatoid arthritis, and severe knee deformity. The same physician performed all procedures to ensure consistency in the treatment.

2.2. Patient demographics

From an initial cohort of 180 patients treated between September 2017 and February 2022, 12 were excluded based on the exclusion criteria, leaving 125 and 43 patients in the SVF and MFAT groups, respectively. Using 1:1 propensity-score matching based on age, sex, body mass index (BMI), and KL classification, the two groups were balanced with respect to these background characteristics, resulting in 36 patients per group for the final analysis (Fig. 1, Table 1).

2.3. SVF and MFAT extraction

In this study, adipose tissue (100–360 mL) was harvested under general anesthesia from the abdominal or buttock regions using two distinct methods: the Lipogems® system (Lipogems International SpA, Milan, Italy) and the Celution® 800/CRS system (Cytori Therapeutics Inc., San Diego, CA).

2.3.1. SVF-cell isolation using the Celution® 800/CRS system

The adipose tissue was washed, followed by enzymatic digestion using Celase® GMP—a blend of collagenase and neutral protease enzymes. The tissue was incubated at approximately 37 °C for 20 min with continuous agitation. After digestion, SVF cells were concentrated, enzymatic residues were removed, and the solution was adjusted to 5 mL with lactated Ringer's solution containing 2.5×10^7 cells.

2.3.2. MFAT preparation using the Lipogems® system

The harvested tissue was mechanically micronized to preserve cellular and structural integrity without enzymatic intervention. The tissue was washed in a closed sterile system to remove blood and debris. The administered MFAT volume varied, with the average being approximately 11.1 ± 3.54 mL, based on patient-specific needs.

Both processes used clinical-grade solutions and aseptic techniques. Cell viability and counts were assessed using the NC-100™ NucleoCounter® (Chemometec, Allerod, Denmark), an image cytometer using propidium iodide staining.

Table 1
Patient demographic data after propensity-score matching.

Patient Characteristics		SVF $n = 36$	MFAT $n = 36$	p-value
Mean age, y ± SD		71.2 ± 9.5	73.1 ± 9.5	0.43
Male/female		9/27	9/27	1
Mean height, cm ± SD		156.3 ± 10.1	153.7 ± 7.4	0.23
Mean weight, kg ± SD		64.1 ± 9.5	61.2 ± 13.9	0.30
Mean BMI, kg/m2 ± SD		26.3 ± 2.5	25.6 ± 4.4	0.42
Kellgren-Lawrence grade (%)	1	0 (0.0)	1 (2.8)	0.87
	2	3 (8.3)	3 (8.3)	
	3	24 (66.7)	21 (58.3)	
	4	9 (25.0)	11 (30.6)	
Preoperative mean VAS, mm ± SD		56.5 ± 18.8	53.7 ± 26.1	0.61
Mean HKA, degrees ± SD		6.7 ± 5.4	5.9 ± 6.2	0.76

Baseline characteristics of the SVF and MFAT groups, including age, sex, BMI, and KL classification, were matched using 1:1 propensity-score matching. Differences in continuous variables were assessed using the Mann-Whitney *U* test, and categorical variables were analyzed using the Chi-squared test. Values are presented as mean ± SD or percentages where appropriate. SVF, stromal vascular fraction; MFAT, micro-fragmented adipose tissue; BMI, body mass index; VAS, visual analog scale; SD, standard deviation.

2.4. Clinical outcomes

2.4.1. Primary outcomes

The primary outcome of this study was the change in pain intensity measured using VAS. The VAS is a unidimensional measure of pain intensity, which has been widely used and consists of a 100-

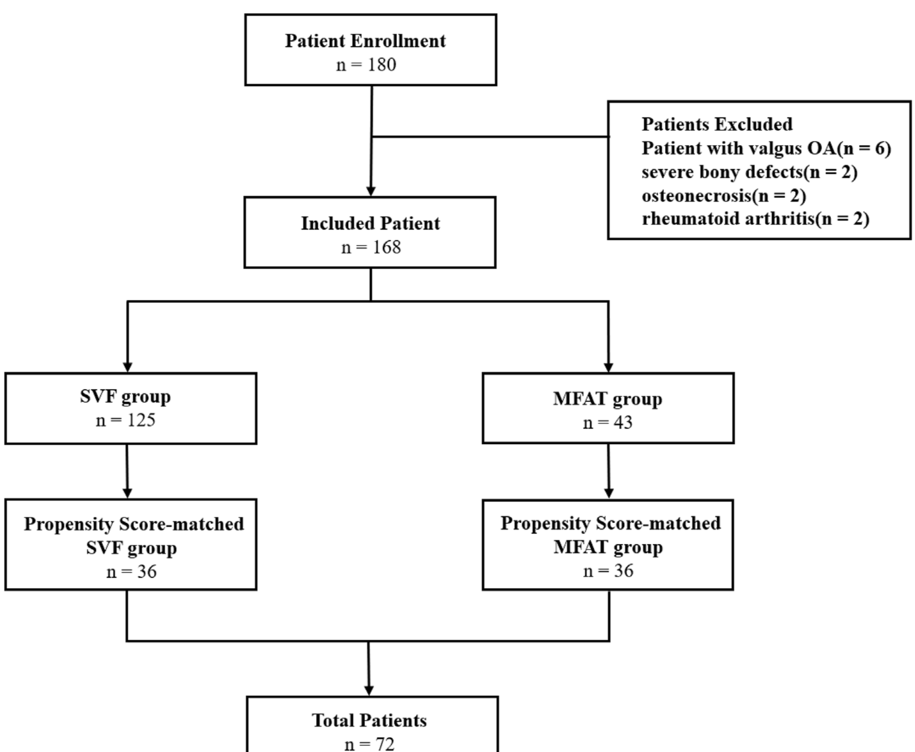

Fig. 1. Flow chart of patient investigation with propensity-score matching. OA, osteoarthritis; MFAT, micro-fragmented adipose tissue; SVF, stromal vascular fraction.

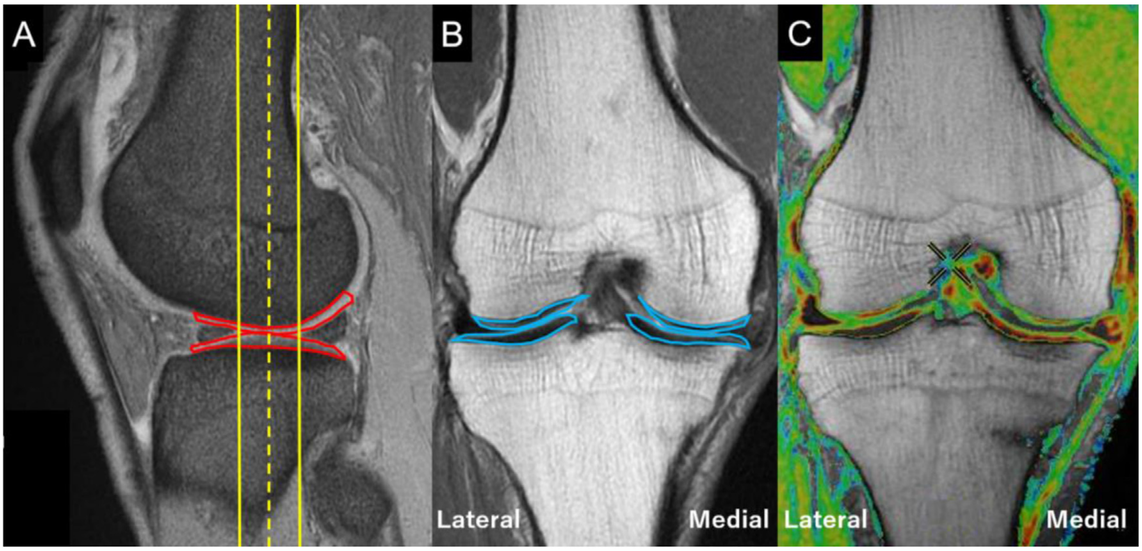

Fig. 2. Method of Calculating the T2 Mapping Value of Cartilage. (A) In a sagittal T1-weighted MR image, a central slice (yellow dotted line) was selected to pass through the center of the weight-bearing cartilage (red line), which is positioned between the anterior and posterior margins of the meniscus. Additionally, two adjacent slices were included, located anteriorly and posteriorly to the central slice (yellow solid lines). (B) In the corresponding coronal T2-weighted MR image at the level of the central slice, regions of interest (ROI) were delineated (blue lines) in the cartilage of the medial and lateral femoral condyles, as well as the medial and lateral tibial plateaus. (C) In the coronal T2 map MR image, T2 mapping values were obtained by analyzing the predefined ROI positions. MR: magnetic resonance.

mm line ranging from "no pain" (0 mm) to "worst imaginable pain" (100 mm). The patients marked their level of pain on the line, and the score was measured from the left end of the line to the point marked by the patient. Pain levels were assessed preoperatively and at 1, 3, 6, and 12 months postoperatively during patient visits to the hospital, where clinical assessments and the collection of any adverse events were conducted.

2.4.2. Secondary outcomes

Knee injury and osteoarthritis outcome score (KOOS): The KOOS is a patient-reported outcome-measurement instrument used extensively in knee OA. The score covers five dimensions: pain, other symptoms, function in activities of daily living (ADL), function in sport and recreation (sports), and knee-related quality of life (QOL) [13]. KOOS was assessed preoperatively and at 1, 3, 6, and 12 months postoperatively. In addition to individual subscale scores, Total KOOS Score was calculated as the mean of the five subscale scores.

Range of motion (ROM): The knee ROM was quantified using a goniometer during flexion and extension. This measurement provides insights into the functional status of the knee joint. ROM was assessed preoperatively and at 1, 3, 6, and 12 months postoperatively.

Knee muscle strength: Muscle strength was assessed as the force generated during knee flexion and extension, normalized to body weight, and reported as Newton per kilogram (N/kg). This assessment evaluates muscular health and rehabilitation progress after treatment. Knee muscle strength was assessed preoperatively and at 1, 3, 6, and 12 months postoperatively.

Responder rate: This composite index was used to determine overall treatment success based on improvements in pain, function, and global assessment score. According to the Outcome Measures in Rheumatology-Osteoarthritis Research Society International (OMERACT-OARSI) criteria [14], to qualify as a responder, a patient must have shown either a minimum of 50 % improvement in pain or function with an absolute change of at least 20 on a 0–100 scale, or a minimum of 20 % improvement in two of the three categories (pain, function, or global assessment), with at least one of these improvements being at least 10 units on a 0–100 scale.

Magnetic resonance imaging T2 mapping: Measurements were conducted based on previous studies [15,16]. To calculate T2-mapping values, a sagittal slice from T1-weighted fast-field echo images that passed through the center of the weight-bearing cartilage delineated by the anterior and posterior margins of the meniscus was selected (Fig. 2). In addition to this central slice, two adjacent slices, one anterior, and one posterior, were analyzed. Regions of interest (ROI) were established on the weight-bearing, full-thickness cartilage of the medial and lateral femoral condyles and the medial and lateral tibial plateaus on the central coronal slice. The same method was applied to the anterior and posterior slices. T2-mapping values from 12 ROIs were recorded, with lower values indicating a lower degree of articular cartilage degeneration. T2 mapping was assessed preoperatively and at 12 months postoperatively.

2.5. Statistical analysis

Propensity-score matching was used to ensure similarity in baseline characteristics between the SVF and MFAT groups. This was conducted using logistic regression based on variables such as age, sex, BMI, and KL classification using EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan). Hypothesis testing was conducted using the Mann–Whitney *U* test, Chi-squared test, repeated-measures analysis of variance, and generalized estimating equations, with a critical *p*-value of 0.05 denoting statistical significance. For the main effect of time in the repeated-measures analysis of variance, Mauchly's test for sphericity was performed, and the Greenhouse-Geisser correction was applied when the assumption of sphericity was violated.

3. Results

3.1. VAS

Significant improvements in VAS were observed in both the SVF and MFAT groups at all time points after treatment, indicating effective postoperative pain reduction (SVF: 56.5 ± 18.8 to 38.5 ± 25.3 mm, $p < 0.01$; MFAT: 53.7 ± 26.1 to 33.5 ± 27.3 mm,

Table 2
Changes in VAS and KOOS domains before and after treatment.

	SVF	p - value	MFAT	p - value	p - value SVF vs MFAT	p - value Group × Time
VAS(mm)						
Preoperative	56.5 ± 18.8		53.7 ± 26.1			0.71
1 month	37.0 ± 21.9	<0.01	39.5 ± 24.8	0.11		
3 months	36.8 ± 24.8	<0.01	35.1 ± 23.5	<0.01	0.74	
6 months	35.7 ± 26.3	<0.01	35.0 ± 27.2	0.02		
12 months	38.5 ± 25.3	<0.01	33.5 ± 27.3	<0.01		
Knee injury and osteoarthritis outcome score						
Pain						
Preoperative	52.9 ± 15.8		48.5 ± 19.2			0.16
1 month	60.6 ± 17.8	<0.01	55.7 ± 17.4	0.16		
3 months	61.3 ± 17.7	0.10	63.7 ± 19.4	<0.01	0.61	
6 months	62.3 ± 17.8	0.11	63.0 ± 21.3	<0.01		
12 months	64.3 ± 15.6	<0.01	60.6 ± 23.3	<0.01		
Symptom						
Preoperative	65.6 ± 18.4		63.4 ± 17.3			0.59
1 month	68.3 ± 19.3	1.0	62.5 ± 16.5	1.0		
3 months	68.3 ± 22.9	1.0	68.6 ± 17.0	0.74	0.92	
6 months	67.2 ± 19.7	1.0	62.0 ± 16.9	1.0		
12 months	68.7 ± 14.1	1.0	65.4 ± 17.8	1.0		
ADL						
Preoperative	70.4 ± 18.6		66.3 ± 18.8			0.95
1 month	77.0 ± 14.9	0.01	72.2 ± 17.1	0.21		
3 months	78.1 ± 16.0	0.11	74.1 ± 19.1	0.01	0.21	
6 months	78.3 ± 16.7	0.21	72.9 ± 18.9	0.07		
12 months	76.3 ± 16.1	0.69	72.3 ± 19.1	0.14		
Sports						
Preoperative	32.9 ± 24.3		23.6 ± 18.5			0.15
1 month	39.7 ± 22.3	0.49	30.3 ± 21.1	0.07		
3 months	40.6 ± 24.5	0.71	33.5 ± 20.6	<0.01	0.16	
6 months	40.4 ± 22.5	0.90	40.4 ± 26.1	<0.01		
12 months	39.0 ± 24.6	1.0	31.7 ± 25.6	0.08		
QOL						
Preoperative	33.3 ± 22.0		29.7 ± 16.0			0.95
1 month	40.6 ± 18.8	0.12	35.2 ± 15.2	0.34		
3 months	44.6 ± 18.8	0.11	37.8 ± 17.2	0.11	0.17	
6 months	45.1 ± 22.3	0.04	39.6 ± 19.1	0.03		
12 months	43.2 ± 26.7	0.21	38.2 ± 18.3	0.08		
Total KOOS						
Preoperative	42.2 ± 14.4		38.2 ± 11.7			
1 month	47.4 ± 13.3	0.01	42.4 ± 12.7	0.21		
3 months	48.6 ± 13.6	0.2	45.9 ± 12.8	<0.01	0.20	0.79
6 months	48.7 ± 14.6	0.18	46.1 ± 15.0	<0.01		
12 months	48.4 ± 14.6	0.21	44.4 ± 15.0	<0.01		

This table summarizes the changes in visual analog scale (VAS) scores for pain and knee injury and osteoarthritis outcome score (KOOS) domains—pain, activities of daily living (ADL), Sports, quality of life (QOL), and symptoms—at preoperatively and at 1, 3, 6, and 12 months postoperatively. Within-group differences were analyzed using repeated-measures analysis of variance (ANOVA) to assess changes over time within each group. The *p*-values for SVF vs MFAT represent the overall group differences, while the *p*-values for Group × Time indicate whether the treatment response patterns differ over time. SVF, stromal vascular fraction; MFAT, micro-fragmented adipose tissue.

$p < 0.01$) (Table 2). However, there was no significant difference in treatment effects between the two groups (SVF vs MFAT, $p = 0.74$), nor was there a significant interaction effect over time (SVF vs MFAT × Time, $p = 0.71$).

3.2. Adverse events

No serious adverse events, as defined by the International Conference of Harmonisation guidelines, were observed in either the MFAT or SVF groups. Mild and transient pain or swelling at the injection and fat harvesting sites was reported in both groups, with symptoms resolving within two weeks with standard pain relief. There were no significant differences in the adverse event profiles between the two groups. There were no reports of complications such as limited knee range of motion, fat embolism, deep vein thrombosis, intra-articular infection leading to sepsis, knee adhesions following SVF injection, superficial infection or intra-articular bleeding in either group during the follow-up period.

3.3. KOOS

Significant improvements were observed in Pain, ADL, and QOL in both groups (Table 2). Pain improved significantly at 1 and 12 months in the SVF group ($p < 0.01$), while the MFAT group showed significant improvements at 3, 6, and 12 months ($p < 0.01$). However, there were no significant differences in pain reduction between the two groups at any time point ($p = 0.61$ at 3 months). ADL showed sustained improvements postoperatively, with significant improvement at 1 and 3 months (SVF: $p = 0.01$ at 1 month; MFAT: $p = 0.01$ at 3 months), but no significant differences between the groups. QOL improved progressively in both groups, with significant improvement from 6 months onward in SVF ($p = 0.04$ at 6 months) and MFAT ($p = 0.03$ at 6 months). However, no significant differences were found between the groups. Symptoms remained largely unchanged in both groups, with no significant deterioration or improvement observed at any time point. Sports improved significantly in the MFAT group at 3 and 6 months ($p < 0.01$),

Table 3
Changes in ROM and knee-muscle strength before and after treatment.

	SVF	p - value	MFAT	p - value	p - value SVF vs MFAT	p - value Group × Time
Range of motion of the knee(°)						
Extension						
Preoperative	−7.1 ± 7.3		−8.5 ± 7.0			0.88
1 month	−4.9 ± 5.3	<0.01	−6.3 ± 5.7	<0.01		
3 months	−4.7 ± 5.3	<0.01	−6.0 ± 5.8	<0.01	0.34	
6 months	−4.4 ± 4.7	<0.01	−5.1 ± 5.0	0.06		
12 months	−3.9 ± 4.5	<0.01	−5.0 ± 5.5	0.04		
Flexion						
Preoperative	130.0 ± 16.1		126.1 ± 16.8			0.03
1 month	132.5 ± 17.1	<0.01	129.9 ± 16.7	0.21		
3 months	132.5 ± 18.1	<0.01	132.8 ± 14.6	<0.01	0.85	
6 months	132.5 ± 15.0	<0.01	133.2 ± 14.3	<0.01		
12 months	131.9 ± 15.0	0.39	129.9 ± 14.4	0.01		
Muscle force (Nm/Kg)						
Extension(quadriceps)						
Preoperative	3.4 ± 1.1		3.1 ± 1.1			0.29
1 month	4.0 ± 1.2	1.0	3.2 ± 1.0	1.0		
3 months	3.4 ± 1.4	1.0	3.3 ± 1.1	0.20	0.95	
6 months	3.4 ± 1.3	1.0	3.6 ± 1.5	0.1		
12 months	3.3 ± 1.6	1.0	3.7 ± 1.2	<0.01		
Flexion (Hamstrings)						
Preoperative	1.8 ± 0.6		1.7 ± 0.5			0.35
1 month	1.7 ± 0.6	1.0	1.8 ± 0.5	1.0		
3 months	1.6 ± 0.5	0.43	1.8 ± 0.6	1.0	0.56	
6 months	1.7 ± 0.6	1.0	1.9 ± 0.6	0.16		
12 months	1.9 ± 1.0	1.0	1.9 ± 0.6	0.11		

This table presents the changes in range of motion (ROM) and knee-muscle force at preoperatively and at 1, 3, 6, and 12 months postoperatively for the MFAT and SVF groups. Within-group differences were analyzed using repeated-measures analysis of variance (ANOVA) to assess changes over time within each group. The *p*-values for SVF vs MFAT represent the overall group differences, while the *p*-values for Group × Time indicate whether the treatment response patterns differ over time. SVF, stromal vascular fraction; MFAT, micro-fragmented adipose tissue.

whereas no significant changes were observed in the SVF group. However, no significant between-group differences were detected (SVF vs MFAT, $p = 0.16$). The Total KOOS, calculated as the mean of all subscale scores, improved in both groups but did not show significant differences over time.

3.4. ROM and muscle strength

3.4.1. ROM and muscle strength

The SVF group showed significant flexion angle improvement from 1 to 6 months postoperatively, but experienced slight deterioration at 12 months ($p = 0.39$). The MFAT group, in contrast, demonstrated significant improvement from 3 months, with sustained benefits at 12 months ($p < 0.01$). Although no overall difference was found between the groups, a significant interaction effect for Group × Time ($p = 0.03$) suggests that the early effects in the SVF group and the sustained benefits in the MFAT group contributed to this interaction (Table 3). Both groups showed significant improvements in extension angle with no significant differences between them. Regarding extension muscle strength, the SVF group exhibited a trend toward improvement without statistical significance, whereas the MFAT group showed significant improvement only at 12 months. Flexion muscle strength showed a similar trend in both groups, but no statistically significant changes were observed.

3.5. T2 mapping

T2-mapping revealed considerable improvements in cartilage preservation across almost all tested areas in both groups (Table 4). Notably, the MFAT group exhibited greater improvement than the SVF group in several specific areas, including the anterior and mid-lateral regions of the femoral condyle, as well as the mid-lateral and posterior-lateral regions of the tibial plateau.

3.6. OMERACT-OARSI responder rate

Responder rates differed between treatments (Fig. 3). The SVF group exhibited notable improvement early in the treatment process; however, the effects declined gradually. In contrast, the response rate in the MFAT group showed an increasing trend from six months to one year after treatment. However, no significant differences were observed in the overall results between the two groups ($p = 0.11$).

4. Discussion

This study demonstrated that both SVF and MFAT treatments effectively improved pain, joint function, and cartilage quality in knee OA patients, consistent with findings from previous studies [7–9,17]. SVF provided rapid symptomatic relief, but its effects were relatively short-term, whereas MFAT resulted in gradual and sustained improvements, particularly in joint function and cartilage preservation. T2 mapping analyses further revealed superior cartilage quality in the lateral compartment in the MFAT group, supporting its structural preservation properties. These findings suggest that SVF is beneficial for early-stage symptom management, while MFAT offers long-term benefits, especially in more advanced cases.

The rapid symptom relief observed with SVF treatment is likely attributed to its strong anti-inflammatory properties, which effectively reduce synovial inflammation—one of the key drivers of OA progression [18,19]. SVF contains a heterogeneous mix of cells, including endothelial cells, pericytes, fibroblasts, macrophages, and adipose-derived stem cells, enabling a multifaceted approach to

Table 4
Comparison of T2 Mapping values in various knee joint regions.

Locations within the Knee joint		SVF $n = 36$	MFAT $n = 36$	p-value SVF vs MFAT
Anterior medial femur	Preoperative	51.10 ± 2.57	52.14 ± 3.61	
	1Y after surgery	50.26 ± 2.43	50.16 ± 3.33	0.887
	Pre vs 1Y p-value	0.157	0.018[b]	
Anterior medial tibia	Preoperative	43.18 ± 2.71	43.90 ± 3.83	
	1Y after surgery	39.54 ± 2.46	39.45 ± 3.12	0.883
	Pre vs 1Y p-value	<0.001[b]	<0.001[b]	
Anterior lateral femur	Preoperative	43.91 ± 1.90	43.80 ± 4.03	
	1Y after surgery	42.17 ± 2.13	40.34 ± 3.45	0.008[a]
	Pre vs 1Y p-value	<0.001[b]	<0.001[b]	
Anterior lateral tibia	Preoperative	39.43 ± 3.12	39.61 ± 3.97	
	1Y after surgery	37.34 ± 2.95	36.43 ± 4.65	0.321
	Pre vs 1Y p-value	0.005[b]	0.003[b]	
Central medial femur	Preoperative	51.72 ± 2.54	52.31 ± 3.36	
	1Y after surgery	49.75 ± 2.64	50.04 ± 2.98	0.667
	Pre vs 1Y p-value	0.002[b]	0.003[b]	
Central medial tibia	Preoperative	42.74 ± 2.95	42.90 ± 4.09	
	1Y after surgery	38.46 ± 1.99	39.35 ± 3.41	0.178
	Pre vs 1Y p-value	<0.001[b]	<0.001[b]	
Central lateral femur	Preoperative	47.32 ± 2.75	47.41 ± 4.32	
	1Y after surgery	46.48 ± 2.57	44.48 ± 5.28	0.044[a]
	Pre vs 1Y p-value	0.187	0.012[b]	
Central lateral tibia	Preoperative	37.39 ± 3.55	37.08 ± 2.22	
	1Y after surgery	37.05 ± 3.17	35.55 ± 3.18	0.048[a]
	Pre vs 1Y p-value	0.671	0.02[b]	
Posterior medial femur	Preoperative	52.23 ± 2.63	52.16 ± 5.62	
	1Y after surgery	51.25 ± 2.41	51.75 ± 4.04	0.526
	Pre vs 1Y p-value	0.104	0.721	
Posterior medial tibia	Preoperative	42.32 ± 2.85	42.13 ± 4.52	
	1Y after surgery	38.30 ± 2.94	38.39 ± 4.18	0.912
	Pre vs 1Y p-value	<0.001[b]	0.001[b]	
Posterior lateral femur	Preoperative	47.16 ± 2.30	46.33 ± 4.54	
	1Y after surgery	43.33 ± 1.99	43.03 ± 4.32	0.705
	Pre vs 1Y p-value	<0.001[b]	0.002[b]	
Posterior lateral tibia	Preoperative	37.57 ± 2.70	37.12 ± 3.43	
	1Y after surgery	36.93 ± 3.61	34.55 ± 3.46	0.006[a]
	Pre vs 1Y p-value	0.395	0.002[b]	

Data are presented as mean ± standard deviation. Differences between the SVF and MFAT groups were analyzed using the Mann-Whitney U test, while changes compared with preoperative outcomes were assessed using the Wilcoxon signed-rank test.
[a] Statistically significant difference between SVF and MFAT groups.
[b] Statistically significant compared with preoperative outcome. SVF, stromal vascular fraction; MFAT, micro-fragmented adipose tissue.

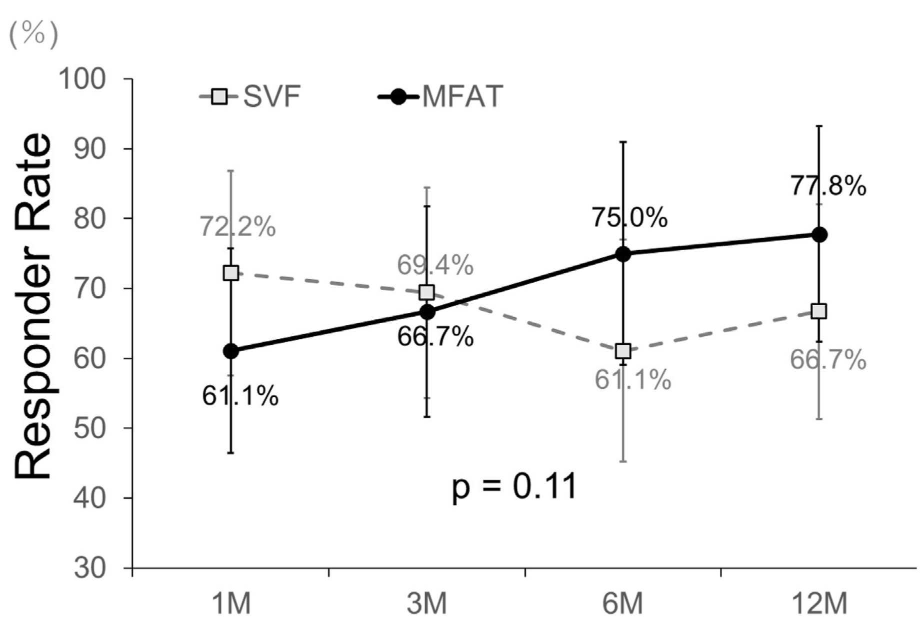

Fig. 3. OMERACT-OARSI responder rate in patients receiving intra-articular injection of MFAT and SVF cells. Responder rates at 1, 3, 6, and 12 months for SVF and MFAT groups. Generalized estimating equations were used to analyze the data. Error bars represent 95 % confidence intervals. MFAT, micro-fragmented adipose tissue; SVF, stromal vascular fraction; OMERACT-OARSI, Outcome Measures in Rheumatology-Osteoarthritis Research Society International.

immune modulation and tissue repair [18]. Among these, M2 macrophages are particularly important for SVF's rapid anti-inflammatory effects [20]. Fujita et al. and Anjiki et al. demonstrated that M2 macrophages and their associated cytokines, such as TGF-β and IL-10, play a critical role in enhancing SVF's immunomodulatory and therapeutic efficacy [4,21]. These findings align with previous clinical studies reporting early symptomatic improvements following SVF treatment [22,23].

MFAT, on the other hand, demonstrated gradual and sustained improvements in knee OA, including a notable enhancement in the flexion angle. T2 mapping further revealed superior cartilage quality in less-loaded lateral regions, particularly in patients with medial OA. These findings suggest that the structural preservation inherent to MFAT contributes to its prolonged efficacy [7], particularly in non-weight-bearing areas. The retention of adipose tissue architecture allows for the sustained release and localized activity of cytokines and growth factors essential for tissue repair [24,25]. Vezzani et al. [26]. Highlighted MFAT's high pericyte content, which supports vascular stability and creates a regenerative environment. Additionally, Desando et al. [27]. Demonstrated MFAT's potential for cartilage regeneration through its ability to modulate the tissue-repair process effectively. These characteristics make MFAT a promising option for long-term therapeutic applications, consistent with findings reported in clinical studies [28,29].

The differing temporal dynamics observed in this study are partially reflected in the OMERACT-OARSI responder rates, indicating the tendency for rapid but short-term effects with SVF and a trend toward sustained benefits with MFAT. However, these differences were not statistically significant, and further studies with larger sample sizes are needed to confirm these trends. The significant group $\times$ time interaction observed in flexion angle improvements suggests a relationship between treatment type and functional recovery, supporting the distinct therapeutic patterns of SVF and MFAT. These results indicate that SVF may be more suitable for immediate symptom relief, while MFAT could offer long-term benefits for knee OA, particularly in advanced cases. This contrast in therapeutic patterns provides useful insights for clinical decision-making.

This study has limitations. The retrospective design may have introduced bias, though propensity-score matching was applied to balance baseline characteristics. Since OA severity may influence the efficacy of cell therapy, we did not perform a subgroup analysis based on Kellgren-Lawrence (KL) grade, as it was already accounted for in the matching process, and further stratification would have reduced the sample size, limiting statistical power. Additionally, post-injection joint pain and swelling were not systematically assessed, potentially leading to underreporting of mild adverse events. The short-term follow-up also limited insights into the long-term effects of SVF and MFAT. Variability in extraction and preparation techniques may have influenced treatment consistency. Future studies with larger cohorts and longer follow-up periods are needed for more definitive conclusions.

In conclusion, this study highlights the distinct benefits of SVF and MFAT in knee OA treatment. MFAT offers sustained therapeutic effects, making it ideal for long-term cartilage preservation and advanced OA, while SVF provides rapid symptom relief suited for early-stage interventions. These findings, supported by propensity-score matching and comprehensive assessments, underscore the potential of tailored regenerative therapies. Further research is needed to validate these results and optimize treatment strategies.

Statement of informed consent

All the patients provided informed consent for inclusion in the study.

Authors' contributions

T. Maeda analyzed the data, and wrote the paper. T. Matsumoto designed the study and revised the paper. SS and HI performed the experimental study. MT supported the analysis of data. T. Matsushita and RK supervised the study. All authors read and approved the final manuscript.

Data availability statement

The data are available upon request from the corresponding author.

Ethical approval

The present study was approved by the Review Board for Human Research of Sobajima Clinic (reference number: SC002-1 M and SC002-2 M) and the Kobe University Graduate School of Medicine (reference number: 170181).

Statement of human and animal rights

All procedures in this study were conducted in accordance with the Ethics Committee of our institutions.

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Declaration of competing interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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